PROFILE OF MALARIA IN NORTH CHENNAI –

A STUDY OF 250 CASES

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. BRANCH – I GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

MARCH 2007

CERTIFICATE

This is to certify that the dissertation titled "**PROFILE OF MALARIA IN NORTH CHENNAI - STUDY OF 250 CASES**" is the bonafide original work of **DR. D. RAVI SHANKAR** in partial fulfillment of the requirements for **M.D. Branch-I (General Medicine)** Examination of the Tamilnadu DR. M.G.R Medical University to be held in March 2007. The Period of study was from May 2005 to July 2006.

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DECLARATION

I, **DR. D.RAVI SHANKAR,** solemnly declare that dissertation titled **"PROFILE OF MALARIA IN NORTH CHENNAI - STUDY OF 250 CASES "** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during May 2005 to July 2006 under the guidance and supervision of my unit chief **Prof. S.SHIVAKUMAR**, Professor of Therapeutics.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

Place : Chennai.

Date :

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ACKNOWLEDGEMENT

I owe my thanks to the Dean, Govt. Stanley Medical College and Hospital, **Dr. D.R. GUNASEKARAN, M.S.**, FICS,for allowing me to avail the facilities needed for my dissertation work.

I am grateful to **Prof. S. NATARAJAN, M.D.,** Professor and Head of the Department of Medicine, Govt. Stanley Medical College and Hospital for permitting me to do the study and for his encouragement.

I am extremely thankful to my unit chief **Prof.S.SHIVAKUMAR,M.D,** for his valuable guidance and constant help. I would like to express my sincere gratitude to my Assistant Professors **DR.NOORUL AMEEN M.D**, **DR.C.SUKUMAR M.D** for their guidance and encouragement.

I am thankful to **Mr.A.Vengatesan M.sc PGDCA,CCE,,**Lecturer in statistics, clinical epidemiology unit for helping me in statistically analysing the results of the study.

I am also thankful to my colleagues and house officers for their full cooperation and help in this study.

Last but not the least, my sincere thanks to all the patients who co – operated for this study, without whom this study could not have been undertaken .

CONTENTS

INTRODUCTION

Despite effects at vector control, malaria still remains a major public health problem. Malaria remains to be one of the world's most prevalent infectious diseases. About 300 – 500 million cases are reported annually allover the world with a mortality of about 1.1 to 2.7 million. 90% of these cases are reported from Africa. In India, 2.5 to 3 million cases and 1000 deaths of malaria are reported annually. Many consider this is an underestimate. The parasite profile has been changing significantly over the years with a steady increase in percentage of PF cases across the country (50.5% of cases in 2005). Areas with more than 30% of PF cases are categorized as high risk. These include North East India, Orissa, Jharkand, West Bengal, Madhya Pradesh, Maharashtra & Andrapradesh. In Tamil Nadu 70% of malaria cases are reported from Chennai. Malaria is highly prevalent in places from North Chennai like Tondaiarpet, Washermanpet, Royapuram, Harbour, Mannady, Pattalam & Pulianthope. This study was undertaken at Stanley Medical college Hospital which is located in North Chennai. This study deals with clinical and laboratory profile of Malaria in North Chennai.

AIM

To study the clinical profile of Plasmodium Vivax and Plasmodium Falciparum malaria in north Chennai

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

EPIDEMIOLOGY

Malaria is the most important parasitic infection of human beings which still produces considerable morbidity and mortality world wide especially in tropical countries. There are four species of genus plasmodium that infects humans. They are plasmodium vivax, plasmodium palciparum, plasmodium ovale and plasmodium malariae. Though most of the complications and deaths were caused by plasmodium falciparum , plasmodium vivax is also reported to produce complications in the recent past. The dream of eradicating malaria got a set back due to widespread resistance of vectors to various insecticides and the resistance developed by malarial parasites for various drugs. The understanding of immunology against malaria has thrown light into host factors playing major role in pathogenesis of various complications. Development of vaccines is complicated by presence of multiple stages of parasite and high antigenic variation by the plasmodium. In this study various clinical features

and complications of plasmodium vivax and falciparum were analyzed in detail.

About 300 – 500 million cases are reported annually allover the world with a mortality of about 1.1 to 2.7 million.[1] 90% of these cases are reported from Africa. In India, 2.5 to 3 million cases and 1000 deaths of malaria are reported annually.[2] Many consider this is an underestimate. Malaria is prevalent through out the tropics. Plasmodium falciparum predominates in Africa where as plasmodium vivax is more common in India . Plasmodium ovale and malariae were reported mainly from Africa. Malaria is transmitted by Female Anapheline Mosquito. Transmission does not occur in temperature < 16 C or > 33 C and above 2000m Altitudes. In India the main vector is Anapheline stephensi which breeds in wells and stagnant water.

The endemicity of Malaria is defined in terms of spleen rate or parasite rate in children aged 2-9 yrs as follows:

		Spleen/ parasite rate
Hypo endemic	-	0 – 10 %
Meso endemic	-	10% - 50%
Hyper endemic	-	50% - 75%
Holo endemic	-	> 75%

Severe malaria is uncommon in infants because of maternal antibodies and the presence of Hb F which offers innate resistance against malaria. In holoendemic areas, severe anemia and cerebral malaria occurs mainly in

children < 5 yrs of age and seldom occurs in adults as they develop a state of premunition. Where as in hypoendemic areas and areas with unstable transmission, where the immunity is partial , complicated malaria is common among the adults in the form of jaundice, renal failure and multiple organ failure (MODS).[3] In pregnant women MODS is common than cerebral malaria. Malaria can also be transmitted by blood transfusion, needle sharing and transplantation.

RELATIVE INCIDENCE OF COMPLICATIONS

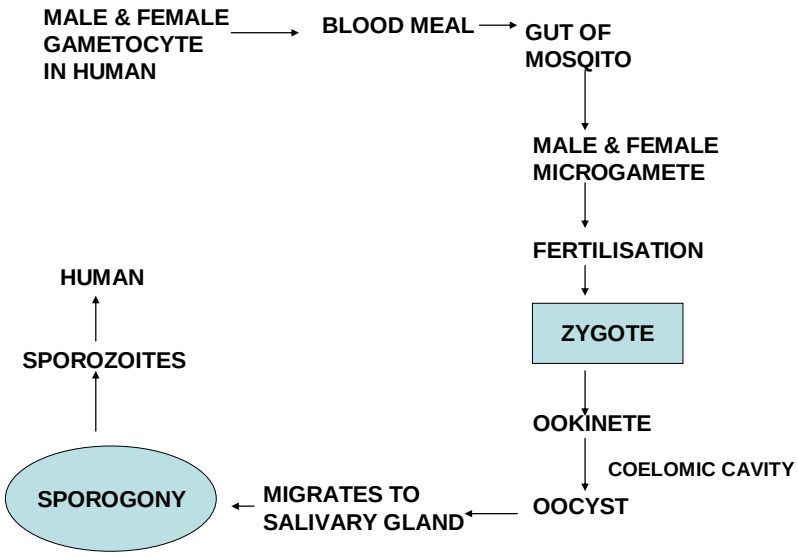
	ADULTS	PREGNANT	CHILDREN
ANEMIA	+	++	+++
CONVULSIONS	+	+	+++
HYPOGLYCEMIA	+	+++	+++
JAUNDICE	+++	+++	+
RENAL FAILURE	+++	+++	-
PUL EDEMA	++	+++	+

LIFE CYCLE OF MALARIAL PARASITE

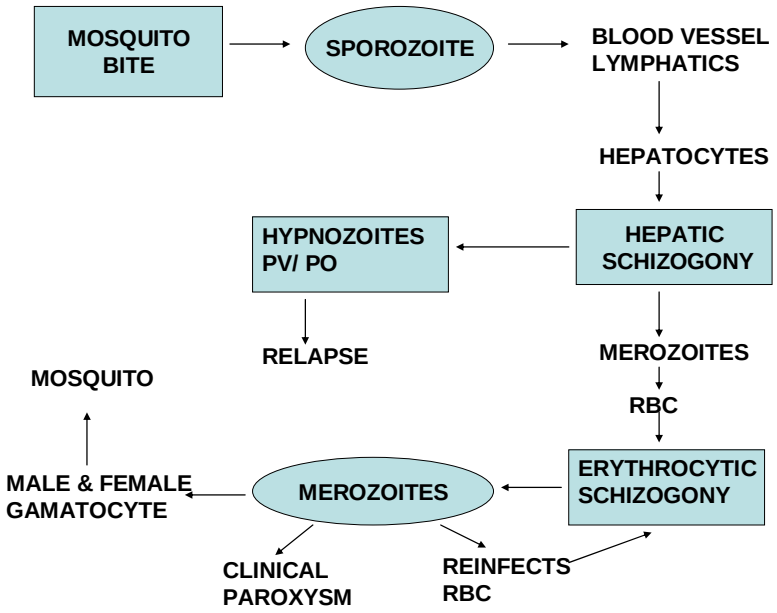
Malarial parasite has two stages of development, sexual and asexual cycle. Mosquito is the definitive host and humans are intermediate host, so sexual cycle (sporogony) occurs in mosquito and asexual cycle (schizogony) in humans. The time taken for the development of malarial parasite in the mosquito is called as extrinsic incubation period. Once the sporozoite enters the

human after the mosquito bite, they reach the liver and hepatic schizogony leads on to release of merozoites, which in turn infects the RBCs. Some merozoites in case of

SEXUAL CYCLE IN MOSQUITO



ASEXUAL CYCLE IN HUMAN BEING



plasmodium vivax and ovale pass in to a stage of exo erythrocytic cycle within the liver which might cause relapse. Erythrocytic schizogony occurs cyclically once in 48 hrs (PV,PO & PF) and 72 hrs in case of plasmodium malariae. The release of merozoites from RBCs co inside with the clinical paroxysm. Thus PV,PF & PO produces fever once in 2 days (tertian malaria) and PM once in 3 days (quartan malaria).

INCUBATION PERIOD:

PLASMODIUM VIVAX - 12 days

PLASMODIUM FALCIPARUM - 09 days

PLASMODIUM OVALE - 15 days

PLASMODIUM MALARIAE - 18 days

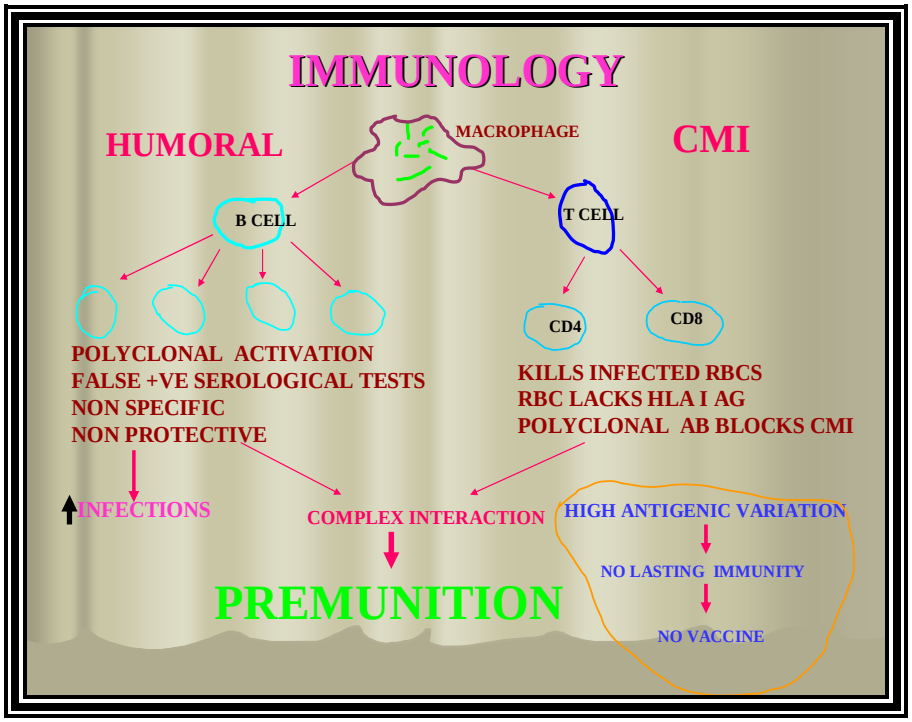
NATURAL PROTECTION AGAINST MALARIA

The following defects in hemoglobin and HLA B 53 protects against malarial disease:

1. Sickle cell trait
2. Melanesian ovulocytosis
3. G6PD deficiency
4. Thalassemia
5. Hemoglobin F
6. HLA B 53

IMMUNOLOGY

Immunity against malaria is highly complex. Non specific immunities against malaria are activation of phagocytes (Neutrophils & Macrophages) and augmentation of splenic clearance (filtration & antibody mediated phagocytosis). Infected RBCs are more rigid and opsonised more easily than uninfected RBCs.



Humoral immune response in malaria is a type of polyclonal B cell activation where there is production of various types of non specific antibodies to various plasmodium antigens. There is a temporary phase of immune suppression that B cells are defective in raising a specific immune response against bacterial infection. So patients with malaria are temporarily prone for bacterial infections like UTI, pneumonia & salmonellosis. More over this polyclonal antibodies block the surface antigens of parasite there by impeding the cell mediated immunity to effectively eliminate the parasite.

Cell mediated immunity plays a major role in controlling the malarial infection as the parasite is a intracellular organism. CD8 cells are the important effector cells in killing the parasite infected RBCs. As the RBCs lack HLA class I antigen and since the parasite undergoes high antigenic variation CD8 cells can not effectively protect against Malaria.

There is a complex interaction between humoral and cell mediated immunity which leads on to a state of premunition where in the immunity against malarial disease persists as long as the host is staying in endemic area and constantly exposed to asymptomatic infection. Once the host moves out of endemic area for a prolonged period, host once again becomes vulnerable for malarial disease. It is interesting to note that AIDS does not worsen malaria. Hence our understanding of immunity against malaria is still unclear.

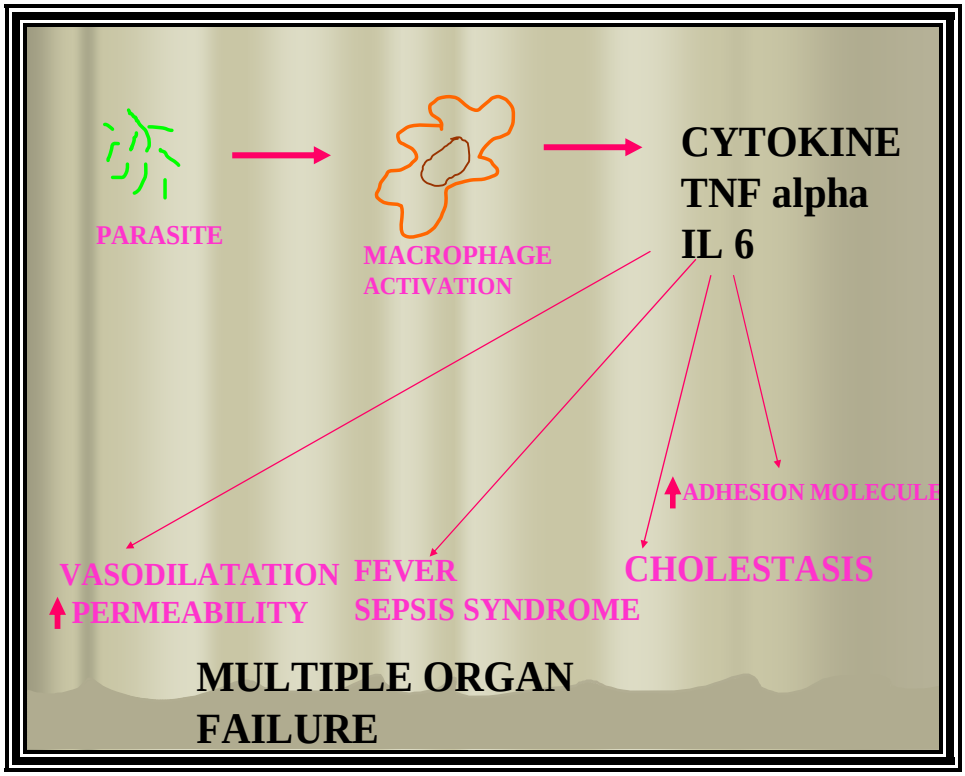
PATHOPHYSIOLOGY

The pathophysiology of malaria results from destruction of RBC, liberation of parasite and erythrocyte material which elicits host reaction.

CYTOKINES

A glycolipid material, similar to bacterial endotoxin released during meront rupture activate monocyte- macrophage and endothelium which in turn leads on to synthesis and release of TNF alpha,[4] IL – 1, IL – 6 and IL – 8. These cytokines are responsible for symptoms and signs of malaria especially fever, malaise, headache and chills. They inhibit gluconeogenesis there by contributing to hypoglycemia. In CNS they stimulate the production of nitric

oxide by cerebral endothelium which inhibits neurotransmisin and leads to coma.



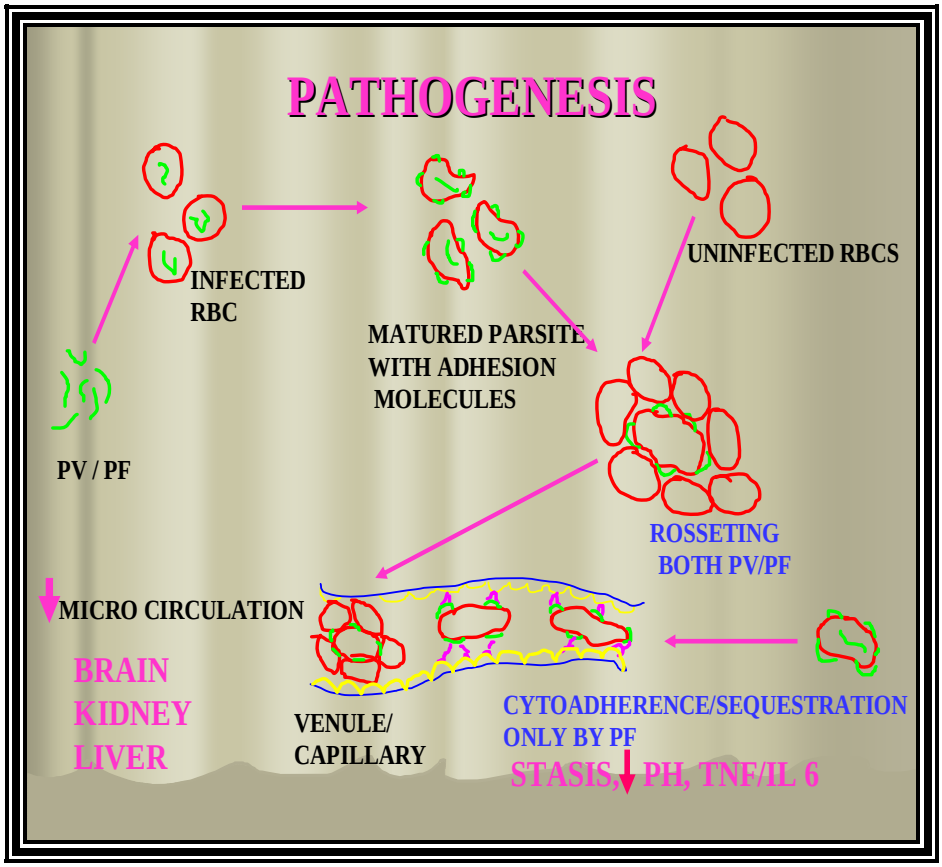
Cytokines upregulates the endothelial adhesion molecules there by favouring cytoadherence. In high concentrations they produce cholestasis, peripheral vasodilatation and shock leading on to Multiple Organ Dysfunction(MODS). They also activates parasite killing by the leucocytes. Thus at appropriate concentration cytokines are protective and when released in high concentrations, they lead on to complications. Thus host factors also play a role in development of complication.

ROSETTING

Erythrocytes containing mature parasite also adhere to uninfected erythrocytes to form Rosettes. Infected RBCs express adhesion molecules in the form of knobs (Hystidine Rich Protein HRP in case of Falciparum)[5] which is capable of binding with CD36 receptors on infected and uninfected RBCs and platelets (CD36 & TSP transpondin) resulting in formation of Rosette. These Rosettes are capable of blocking microcirculation which leads on to stasis, anaerobic glycolysis there by reducing the PH at capillaries which in turn facilitates cytoadherence. Rosetting is encountered in vivax, falciparum and ovale malaria.

CYTOADHERENCE

Cytoadherence is the attachment of infected erythrocytes to vascular endothelium. This phenomenon is exhibited by plasmodium falciparum which expresses PfEMP (Erythrocyte membrane protein) on RBC surface that binds to venular endotheliam through the adhesion molecules CD36, Intercellular Adhesion Molecule -1(ICAM-1),[6] Thrombospondin(TSP), Vascular Endothelial Adhesion Molecule (VCAM) and Endothelial Leucocyte Adhesion Molecule -1(ELAM-1). By cytoadherence, infected RBCs are trapped within the capillaries and venules of various internal organs there by avoiding splenic elimination.

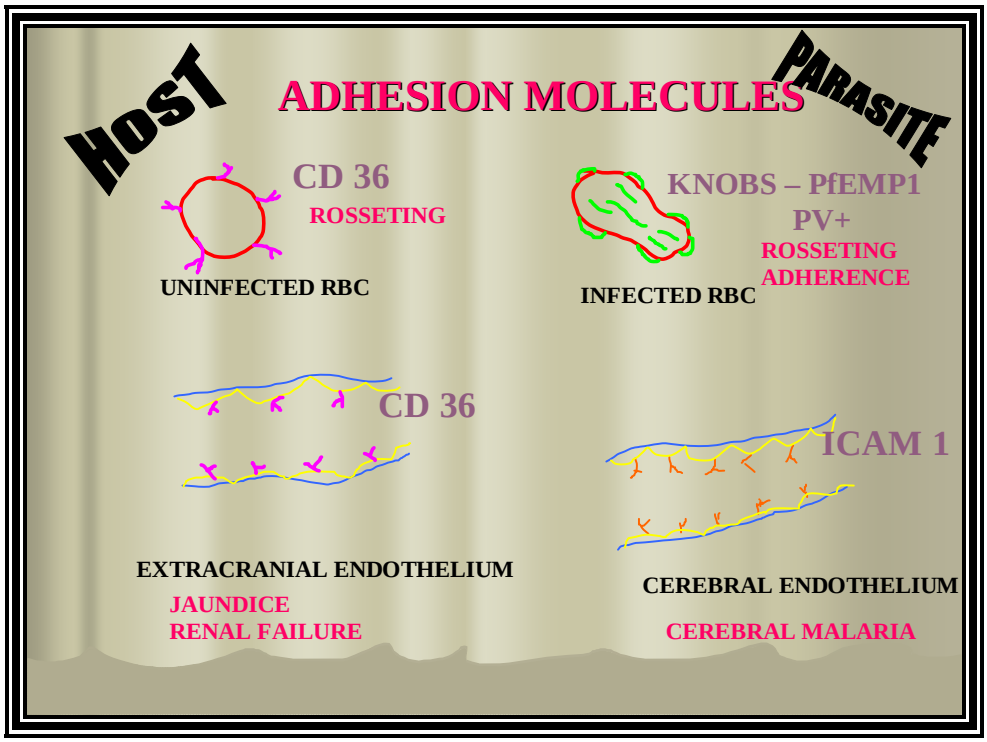


Together Rosetting and Cytoadherence leads on to microcirculatory block and multiple organ dysfunction. In splenectomised animals PF infected RBCs does not exhibit cytoadherence, so spleen might have a modulating role for cytoadherence.

ADHESION MOLECULES ON VASCULAR ENDOTHELIUM

As seen above there are number of endothelial adhesion molecule which binds PfERP. They are CD36, ICAM-1,[6] VCAM & ELAM-1. ICAM-1 appears to be the major vascular ligand in the brain involved in cerebral sequestration and CD36 is the major ligand in other organs. Thus Plasmodium Falciparum

strains with high affinity to ICAM-1 produces cerebral malaria where as strains with affinity to CD36 leads on to MODS.



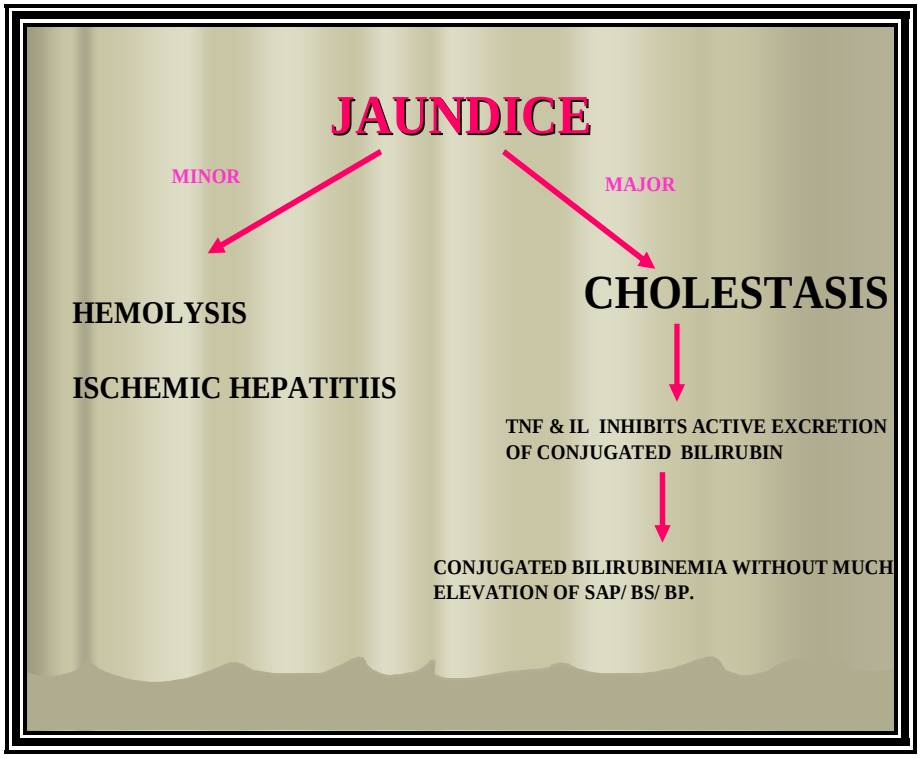
SEQUESTRATION

Through the process of Rosetting and cytoadherence the infected RBCs are trapped within micrvasculature of internal organs. This is called as sequestration. Sequestration leads on to microcirculatory obstruction which results in reduced oxygen & nutrient supply to tissues there by causing anaerobic glycolysis and lactic acidosis.

PATHOGENESIS

1. **JAUNDICE**
    - Hemolysis & increased Bilirubin production.
    - Hepatocyte injury due to ischemic damage caused by microcirculatory block.

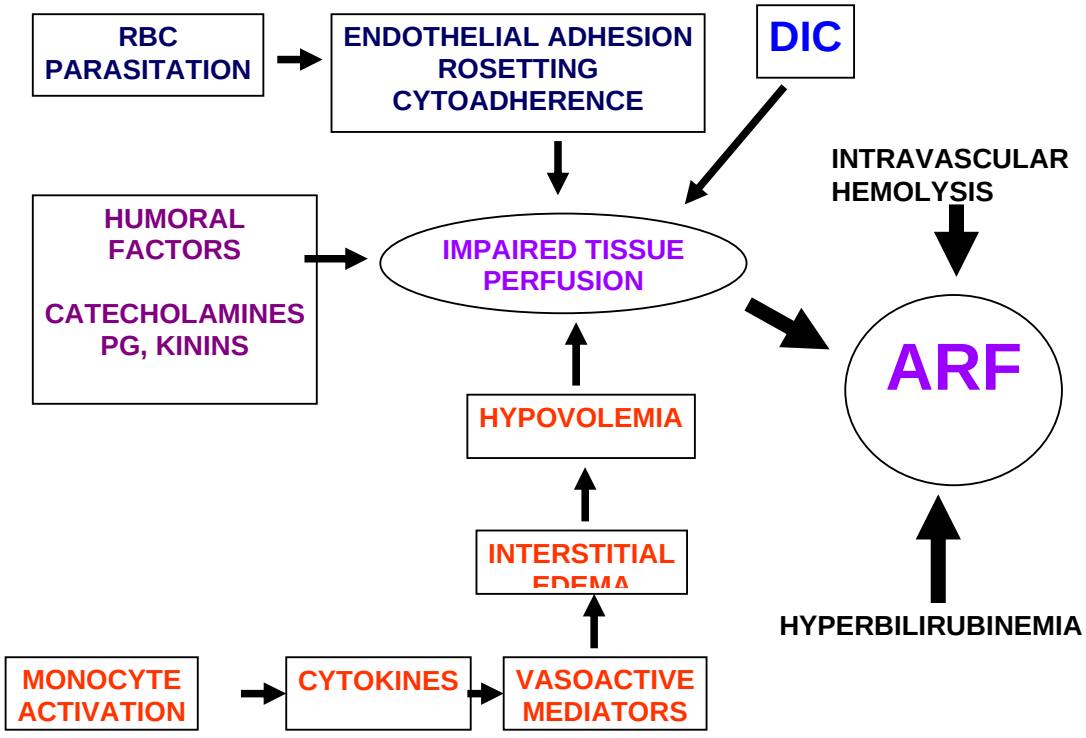
- Cholestasis is major factor leading on to jaundice in malaria. Cytokines inhibits the active excretion of conjugated bilirubin into the biliary canaliculai. So the bilirubinemia is predominantly direct with very mild elevation of transaminases.



2. RENAL FAILURE

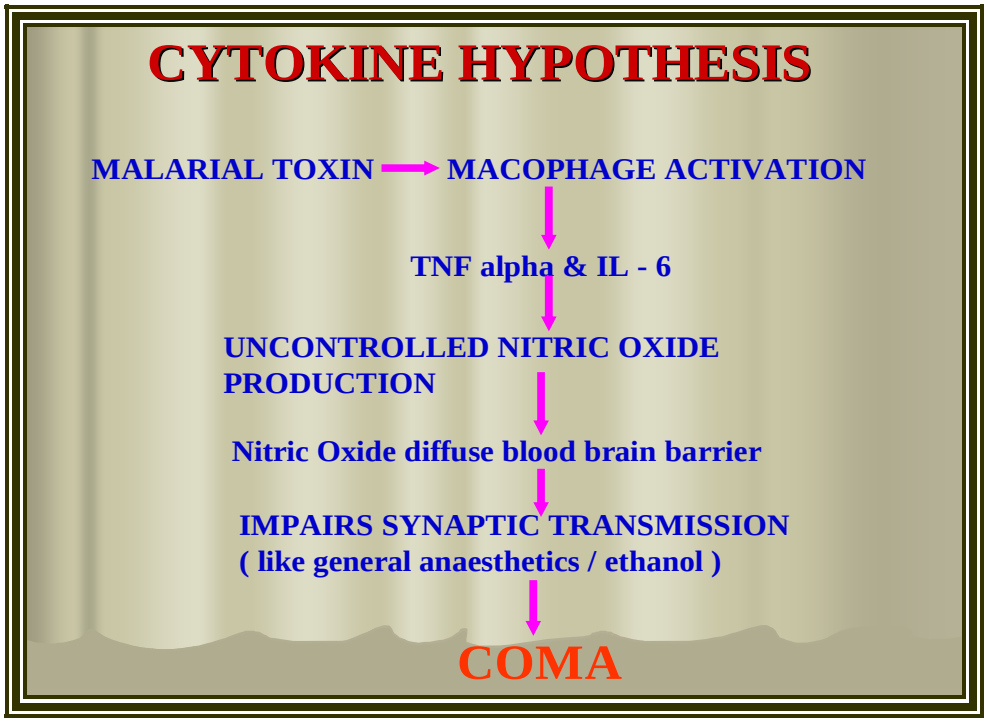
- Microcirculatory (vasa recta) block leading on to ischemic ATN.
- Renal hypoperfusion due to shock secondary to vasodilatation caused by cytokines.

- Hemoglobinuria and Bilirubinuria in Black Water Fever can precipitate ATN.



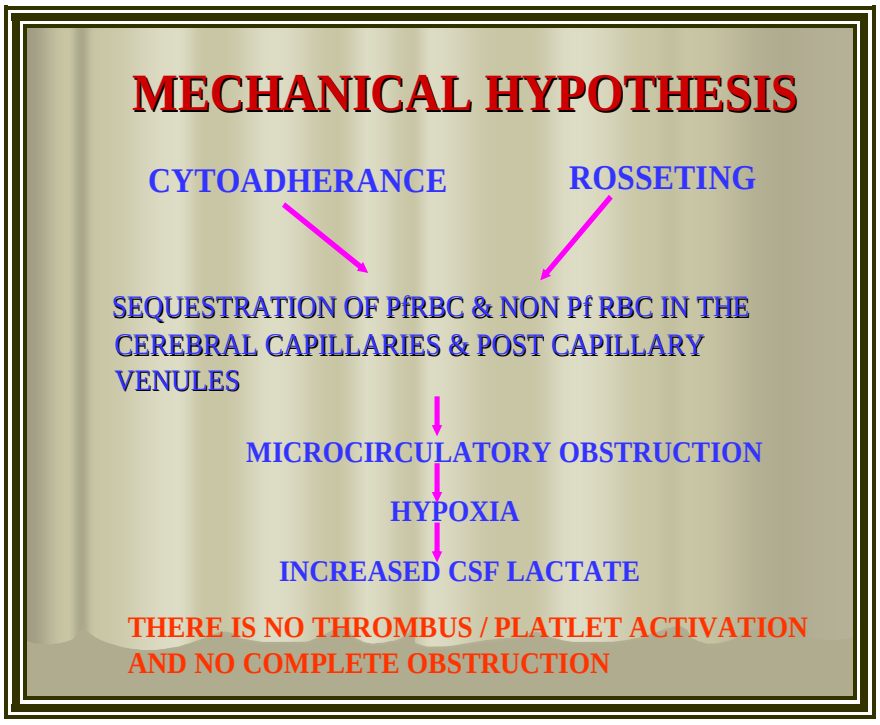
3. CEREBRAL MALARIA

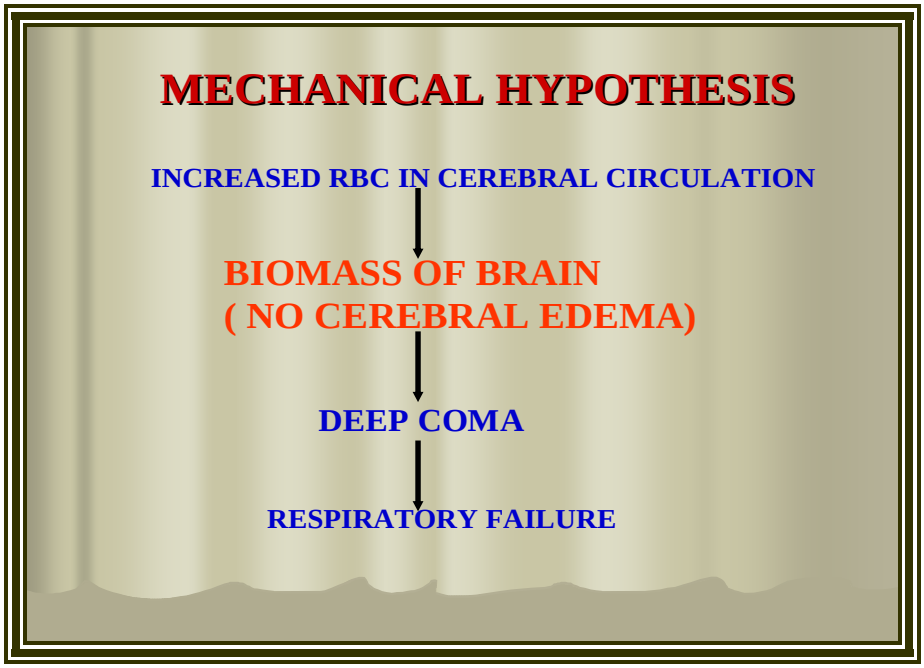
- Increased production of Nitric Oxide by cerebral endothelium induced by cytokines which inhibits neurotransmission.



- Cerebral microcirculatory block leading on to anaerobic glycolysis and CSF lactic acidosis.
- Mechanical hypothesis – increased bio mass of brain due to excessive RBC sequestration especially in children may cause deep coma and respiratory failure.

FLOW CHARTS SHOWING MECHANISMS OF CEREBRAL MALARIA





4. COAGULOPATHY & THROMBOCYTOPENIA

- Thrombocytopenia - Increased destruction of platelets

Decreased synthesis of platelets

Increased consumption in DIC

- Prolongation of PT/ aPTT - increased consumption of clotting factors due to DIC & decreased production by liver.

5. ANEMIA

1. Destruction of parasitized RBCs.
2. Accelerated destruction of non parasitized RBCs.
3. Dys Erythropoiesis.

6. PULMONARY EDEMA

- Increased permeability of alveolar capillary endothelium.

7. HYPOGLYCEMIA

- Increased peripheral utilization of glucose due to anaerobic glycolysis.
- Parasite consumption in hyperparasitemia.
- Failure of hepatic gluconeogenesis and glycogenolysis.
- Quinine induced insulin secretion from pancreatic Beta cells.

8. GIT DYSFUNCTION

- Gut sequestration and visceral vasoconstriction leads on to malabsorption. This may increase the GUT wall permeability leading on to decreased local defence against bacterial invasion.

9. LACTIC ACIDOSIS

- Tissue anaerobic glycolysis due to microcirculatory block.
- Decreased hepatic and renal clearance.
- Increased lactate production by parasites.

CO INFECTION OF VIVAX AND FALCIPARUM

When vivax and falciparum infects same individual at same time usually they don't produce any complications. In vivo, vivax inhibits falciparum and vice versa. So contrary to belief mixed infections are benign.[3]

CLINICAL FEATURES

Incubation periods of four species of plasmodium are different. Clinical features of uncomplicated malaria are common for all four species and are nonspecific. Headache, myalgia, vague abdominal discomfort, lethargy and lassitude often precede fever by up to 2 days. The temperature rises erratically at first with shivering, mild chills, worsening headache, malaise and decreased appetite. If left untreated fever in PV & PO regularizes to a 2 day cycle (Tertian pattern) and plasmodium malariae regularizes to 3 day cycle (quartan pattern). plasmodium falciparum remains erratic for longer period and may never

regularize to a tertian pattern. In an acute paroxysm patient first feels intense headache and muscular discomfort followed by cold and shivering. The temperature rapidly climbs up to a peak of 39-41C, which is followed by profuse sweating. Some patients can have mild abdominal discomfort and diarrhea.

Vivax and ovale malaria have a tendency to relapse weeks or months after primary infection due to exo erythrocytic cycle (Hypnozoites). Plasmodium falciparum is the usual cause of recrudescent malaria and these tend to occur 2-4 weeks after treatment. There is no exo erythrocytic phase in falciparum.

Increased incidence of severe anemia and reduction in birth weight is reported in pregnancies from high endemic areas. Severe malaria has high mortality among pregnant woman compared to non pregnant woman.

DEFINITION OF SEVERE MALARIA BY WHO: The criteria of MODS in malaria are given below

1. Renal failure: Serum Creatinine > = 3mgs/dl
   Urine out put < 400ml/24hrs or <12ml/hr

2. Severe anemia: Hemoglobin <5gms%
   Hematochrit <15%

3. Cerebral malaria: Unarousable coma with peripheral parasitemia

4. Pulmonary edema

5. Hypoglycemia: Blood sugar <40mg/dl

6. Shock: Systolic BP <70mmhg (in adults)
   <50mmhg (in children 1-5 years)

7. Acidemia: PH <7.35, HCO3 <15 mq/L

8. Spontaneous bleeding: gums, nose and GIT due to DIC

9. Macroscopic hemoglobinuria

10. Seizures: More than two episodes

11. Hyperparasitemia: More than 20%

12. Jaundice: serum Bilirubin > 3mgs/dl-marker of severe malaria only when combined with other vital organ dysfunction (cerebral malaria and renal failure)

Impaired consciousness of any degree, jaundice, intractable vomiting and parasitemia > 2% in non immune individuals should be managed as severe malaria.

CEREBRAL MALARIA

Defined strictly as unarousable coma not attributable to any other cause in a patient with plasmodium falciparum. Coma should persists for at least 30 minutes after generalized convulsions. In practice any patient with fever and altered sensorium should be treated as severe malaria. The onset of coma may be sudden following a generalized convulsion or gradual with drowsiness, confusion, disorientation, delirium or agitation. There is no neck rigidity or other signs of meningeal irritation. Neurological manifestations are of symmetrical encephalopathy and focal signs are very rare. Untreated cerebral malaria is uniformly fatal (mortality 15% in children, 20% in adults and 50% in

pregnant woman). Post neurological syndromes occurs in 3% of adults and 10% of children. They are persistent neurological deficit, psychosis, tremor and cerebellar dysfunction. Neurological deficit may be permanent in one fourth of cases.

HEPATIC DYSFUNCTION

Usually of direct bilirubinemia with mild elevation of transaminases is noted. Hepatic failure and encephalopathy are very rare. If hepatic dysfunction is severe prothrombin time may be prolonged.

ACUTE RENAL FAILURE

Usually occurs in adults in areas of low or unstable transmission. Patient may be oliguric or sometimes polyuric. In the fulminant form it is associated with hepatic dysfunction, metabolic acidosis and pulmonary edema. ARF may be associated with hemoglobinuria in patients with massive hemolysis.

ANEMIA

Hemoglobin concentration may fall up to 2 g/dl each day. It is a problem in children which may lead on to high out put cardiac failure (Hb < 4 g/dl).

METABOLIC ACIDOSIS

Kusmaal's breathing suggest metabolic acidosis. This may be due to Lactic acidosis caused by increased anaerobic glycolysis and acute renal failure.

BLACK WATER FEVER

This is due to excessive intravascular hemolysis and hemoglobinuria. Hemoglobin in acidic urine gives black colour to urine. Massive hemoglobinuria leads on to ATN & renal failure. Now a days black water fever is very rare, if occurs it is usually transient and recovers spontaneously.

ACUTE PULMONARY EDEMA

This is a type of Adult Respiratory distress syndrome and may develop at any time in severe plasmodium falciparum malaria. Severe breathlessness and hypoxemia are the main features.

SECONDARY INFECTION

Since malaria is a state of transient immune suppression they are particularly vulnerable for respiratory infection, urinary tract infection and salmonella bacteremia.[3]

DIAGNOSIS OF MALARIA

- **Light microscopy – Thin and Thick Smear**
    - Cost effective, fairly sensitive & highly specific.
    - Thin smear is used for quick diagnosis and thick smear used for species identification.
    - False negative - Very low parasitemia , sequestration of parasitised RBC, technical error.
    - False positive - in highly endemic areas.

- **QBC for malaria (Quantitative Buffy Coat)**
    - Nuclear material of parasite (DNA& RNA) stained with fluorescent dyes and visualized under UV light microscopy. When blood in specialized capillary tube containing acridine orange stain and a float centrifuged, the infected RBC, which have a higher buoyant density than uninfected cells, become concentrated around the float**.** Sensitivity equal or slightly more than thick smear**.**

- **Paracheck- F (Dipstick method)**
    - Detects falciparum specific HRP released from RBCs using monoclonal antibody.
    - Simple and rapid.

- **OptiMAL – Parasite specific LDH detection**

- Sensitivity – 92 to 98%
- Specificity - 92 %

- **Polymerase chain reaction**
  - Highly sensitive
  - Costly and not available easily

LABORATORY ABNORMALITIES

1. Hemogram – Anemia (Normochromic Normocytic Anemia)

   - Leucocytosis > 12,000 may be there.

2. Coagulopathy – Platelets < 50,000 – 100,0000

   PT, a PTT may be prolonged

   Fibrinogen > 200 mg/dl

3. Blood sugar, urea and creatinine.
4. LFT – Total Bilirubin, direct Bilirubin, SGOT, SGPT, SAP.
5. Arterial Blood Gas analysis to see for Acidosis
6. Chest X Ray – ARDS/ LRI
7. Ultrasound Abdomen – Hepatosplenomegaly.

MANAGEMENT

Apart from supportive management like adequate hydration and antipyretics the management strategy for complicated and uncomplicated malaria are different. Once organ dysfunction is noted aggressive management is must to prevent morbidity and mortality.

UNCOMPLICATED MALARIA

Infection due to PV,PO and PM should be treated with oral chloroquine to a total dose of 25 mg/kg (10mg/kg followed by 5mg/kg 6hrs later and daily for two days) over three days. Plasmodium Falciparum should be considered as chloroquine resistant unless the sensitivity is proved and should be treated with Sulfadoxine 1500mg + pyrimethamine 75mg single dose or quinine 10mg 8^{th} hrly with Doxycycline for 5 – 7 days. Mefloquine can also be used to a total dose of 25mg/kg (15mg/kg stat followed by 10mg/kg 12 hrs later). Mefloquine should be combined with Artesunate or artemether for 3 days. Quinine is bitter and may lead on to chinconism. Doxycycline and tetracycline should not be used in pregnancy and children less than 8yrs of age.

To eradicate persistent liver stages and to prevent relapse radical treatment is given in the form of Primaquine 15mg od for 14 days in plasmodium vivax and plasmodium ovale malaria.

Multi drug resistant Plasmodium Falciparum malaria can be treated with quinine, mefloquine, Artemether 20mg+Lumifantrine 120mg total of 6 doses and Atavoquine250mg+proguanil 100mg 4 tablets for 3 days.

COMPLICATED MALARIA

Because of widespread resistance, chloroquine can no longer be relied upon for treatment of severe malaria. Intravenous quinine remains the drug of choice in complicated malaria. Quinine should be given as loading dose of 20mg/kg in D5 or D10 over 4 hrs and the repeated at dose of 10mg/kg in D5 over 4 hrs 8^{th} hrly. Once patient is able to take orally quinine should be given orally in the same dosage to a total of 5 – 7 days. Patient should be monitored for QTc prongation, hypoglycemia and Hypotension during intravenous quinine therapy. In severe renal failure quinine dose should be reduced to half after first 48 hrs.

Alternative therapy for complicated malaria are quinidine gluconate 10mg/kg over 1-2 hrs followed by 0.02mg/kg/min, Artesunate 2.4mg/kg IV followed by 1.2mg/kg daily and Artemether 3.2mg/kg IM followed by 1.6mg/kg/day for 3-5 days.

MALARIA: INDIAN SCENARIO

In 1953 National Malaria Control Programme was launched to curb the menace of malaria which mainly involved spraying of DDT to control the vectors. Due to overwhelming response with a drastic reduction of malaria cases to just 2 lakh cases in the year 1958 NMCP was converted to National Malaria Eradication Programme aimed at eradicating malaria from India. NMEP got a set back in sixties as the incidence of malaria cases was rising alarmingly due to widespread resistance of vector to DDT. With the implementation of Modified plan of operation in 1977, the upsurge of malaria cases dropped down from 6.74 million in 1976 to 2.1 million cases in 1984. Since 1997, there is a declining trend in annual malaria incidence from 3 million in 1996 to 1.65 million in 2003 with 1000 deaths reported annually(gross under estimate).[2]

The major endemic areas in India are North East states, Orissa, Rajasthan, Andhrapradesh, Madhya Pradesh, Gujarat, Jharkand and Chathisgarh. In states like Orissa, Rajasthan and NE states the incidence of PF malaria is increasing at alarming rate especially chloroquine resistant strains. Over all the parasite profile is changing in India with chloroquine resistant PF malaria contributing to more than 50% of cases. Tamil Nadu is a low endemic area which had reported 43,382 cases in 2003 out of which 70% occurred in Chennai.[2] Parasite profile in Chennai was 94.6% PV and 5.4% PF as per corporation of Chennai data.

Recent study from Rajasthan, by Kochar , had revealed a major shift in clinical presentation and complications of falciparum malaria. In 1994 cerebral malaria was the commonest complication encountered and also the commonest cause of death in PF malaria where as in 2001 jaundice , anemia, renal failure and MODS were the commonest presentation of severe malaria and cause of death. This statistically significant shift in presentation of severe malaria from a solitary complication of cerebral malaria in 1994 to MODS in 2001 should alert the physician regarding diagnosis of severe malaria when a patient presents with fever with Jaundice and Renal failure.[8]

MAJOR SHIFT IN PRESENTATION OF FALCIPARUM MALARIA

	1994 (in %)	**2001 (in %)**
• **Jaundice**	11.47	58.85
• **Anemia**	5.83	26.04
• **Bleeding**	9.59	25.54
• **MODS**	9.59	22.40
• **Shock**	5.26	10.94
• **Cerebral malaria**	25.75	10.94
• **Black water fever**	7.89	6.77
• **Renal failure**	2.07	6.25
• **Thrombocytopenia**	0.75	5.73
• **ARDS**	3.01	2.08
• **GCTS**	2.84	1.56

- **Hypoglycemia** 2.07 1.56

When ever severe complications are noted in plasmodium vivax malaria , it is attributed to undetected associated Falciparum malaria. But co infection of PV and PF inhibits each other in vivo and tends to be benign without any complications. Kochar et el in their study of 11 complicated vivax cases with jaundice, renal failure, cerebral malaria , ARDS and bleeding showed the presence of Plasmodium vivax in these patients and confirmed the absence of plasmodium falciparum by doing genetic study (PCR). This study shows that vivax can also produce complications.[9]

In a study of 441 cases of cerebral malaria Kochar et al reported various clinical presentations and post cerebral malaria neurological sequelae as follows:[10]

CEREBRAL MALARIA IN INDIAN ADULTS – A STUDY OF 441 CASES AT BIKANER, NORTH WEST INDIA

CLINICAL PRESENTATION

Fever	-	100%
Unconsciousness	-	100%
Fits	-	21.31%
Neck rigidity	-	19%
Psychosis	-	5.21%
Conjugate Eye deviation	-	2.26%
Extrapyramidal rigidity	-	2.25%

Trismus - 1.31%

Decorticate rigidity - 1.13%

Decerebrate rigidity - 0.90%

They have reported a mortality of 32.37% in cerebral malaria in adults. The commonest neurological sequelae noted were cerebellar ataxia (6.74%), psychosis (5.05%) and aphasia (5.7%). Other associated complications noted in cerebral malaria patients were severe anemia (6.8%), jaundice (6.8%), renal failure (9.07%) and hypoglycemia (4.08%).[10]

Hazra et al reported various clinical profile of malaria in their study of 225 cases (165PV and 60PF) from Calcutta as follows:[11]

Clinical features	**Plasmodium Vivax** (n-165)	**Plasmodium Falciparum** (n – 60)
Classic paroxysm	42.27%	40%
Continuous fever	27.2%	40%
Jaundice	9.09%	40%
Splenomegaly	18.18%	40%
Renal failure	-	5%
ARDS	-	6.6%
GCTS/Coma	-	8.3%
DIC	-	3.3%
Black water fever	-	3.3%

Mohapatra et al from Berhampur has reported various atypical presentations of malaria, in their study of 110 cases of vivax malaria. They were absence of malarial paroxysm(22.8%), migrainous headache (4.5%), myalgia (6.3%), episodic urticarial rash (1.8%), relative bradycardia (13.6%) & postural

hypotension (2.7%). They also noted complications like Jaundice (7.2%), Cerebral malaria (0.9%), severe anemia (7.2%) and thrombocytopenia (3.6%).[12]

The incidence of ARF in malaria is estimated to vary from 1 – 60%. In India, the incidence reported is 17.8% from Delhi, 17.2% from Orissa, 13% from North East India and 5.9% from Mumbai.[13] Profile of ARF in India suggests that malaria contributes 38% of ARF in Orissa and 15.5% in East India (with a increase from 6.6 % in 1995 to 27% in 1999).[14] In Chennai there were no reports of ARF due to malaria before 1995 but since then it has become an important cause of ARF . Jeyakumar et al has reported a incidence of 4.5% malarial ARF in their study of 1112 patients of ARF in Chennai.[15] Plamodium falciparum is the common cause of malarial ARF though also reported with vivax. Prakash et al reported 16.1% of malarial ARF among 577 ARF cases studied, out of which 79.6% is due to PF and 20.4% due to PV.[16] Mehta KS et al from mumbai reported a incidence of 5.9% ARF in their study of 402 cases of malaria 87.5% due to PF and 13.5% caused by PV.[17]

Thus malaria still remains to be a major public health problem in India. The rise in chloroquine resistant strains of Falciparum and the shift in presentation of severe malaria from cerebral malaria to multiple organ dysfunction should alarm the medical authorities and the public health authorities to take necessary steps to control malaria effectively.

PATIENT AND METHODS

1. Patients with fever, from north Chennai admitted to Stanley medical college hospital who were tested positive for plasmodium vivax / falciparum by peripheral smear study (Giemsa) / QBC (Quantitative Buffy Coat) were taken up for the study.
2. All the patients were evaluated for :

   a. Clinical features

   - Intermittent paroxysm
   - Head ache
   - Chills
   - Vomiting
   - Diarrhea
   - Icterus
   - Hepatosplenomegaly
   - Loss of consciousness
   - Convulsions
   - Altered behaviour

   b. Laboratory parameters

   - Hemogram – Hb,TLC, DLC, platelet count,
   - Renal function – Serum urea, creatinine & electrolytes.
   - Blood sugar

- Liver function tests – Total bilirubin, Direct bilirubin, SGOT,SGPT & SAP.
- ECG – to rule out any cardiac abnormality for quinine administration
- Chest X - ray

3. EXCLUSION CRITERIA

Patients with leptospirosis, enteric fever and hepatitis were excluded by doing appropriate investigations. Patients co infected by both plasmodium vivax and falciparum were also excluded from the study.

4. Following criteria were taken to define organ dysfunction in severe malaria:

- Severe anemia - Hb < 8g/dl
- Renal failure - Sr Creatinine - 1.5- 3 mg/dl (mild)
  Sr Creatinine > 3 mg/dl (severe)
- Jaundice - Total Bilirubin – 1.5 -3 mg/dl (mild)
  Total Bilirubin - > 3 mg/dl (severe)
- Cerebral malaria - Loss of Consciousness
  - Altered behaviour / sensorium
  - Generalized Convulsions with no previous history of seizures
- Thrombocytopenia - Platelet count < 1 Lac
- Hypoglycemia - < 60 mg/dl

- ARDS CXR - SiO_2 < 70% (pulse oximeter) with findings and breathlessness

5. Treatment strategy:

- All uncomplicated malaria patients were treated with Chloroquine (25mg/kg) with Doxycycline 100mg bd for 3 days. If there is no clinical response, these patients were switched over to quinine 10mg/kg 8^{th} Hrly.
- All complicated malaria patients showing organ dysfunction were started on quinine 10mg/kg 8^{th} hrly oral or intravenously in dextrose solution along with oral Doxycycline 100mg bd for 7 days.

RESULTS

RESULTS : Total of 250 patients were analysed and the results were :

TOTAL NUMBER OF PATIENTS - 250

NUMBER OF PV - 210 (84%)

NUMBER OF PF - 40 (16%)

NUMBER OF MALES - 170 (68%)

NUMBER OF FEMALES - 80 (32%)

TABLE - 1

AGE AND SEX DISTRIBUTION

AGE RANGE In YRS	**Plasmodium Vivax** (n – 210)		**Plasmodium falciparum** (n-40)%		**TOTAL**
	MALE	FEMALE	MALE	FEMALE	
13 – 20	50	15	3	2	70 (28%)
21 - 30	37	20	7	4	69 (27.6%)
31- 40	16	12	4	3	36 (14.4%)
41 - 50	17	7	5	3	33 (13.2%)
51 - 60	10	2	3	1	16 (6.4%)
61 - 70	10	7	3	1	21 (8.4%)
> 71	5	2	0	1	8 (3.2%)
TOTAL	145(69%)	65(31%)	25 (62.5%)	15(37.5%)	250

MEAN AGE- 27.7 Yrs (RANGE - 13 TO 82 Yrs)

About 70% of patients were in the age group of 13 to 40 years of age. 68% were males and 32% were females.

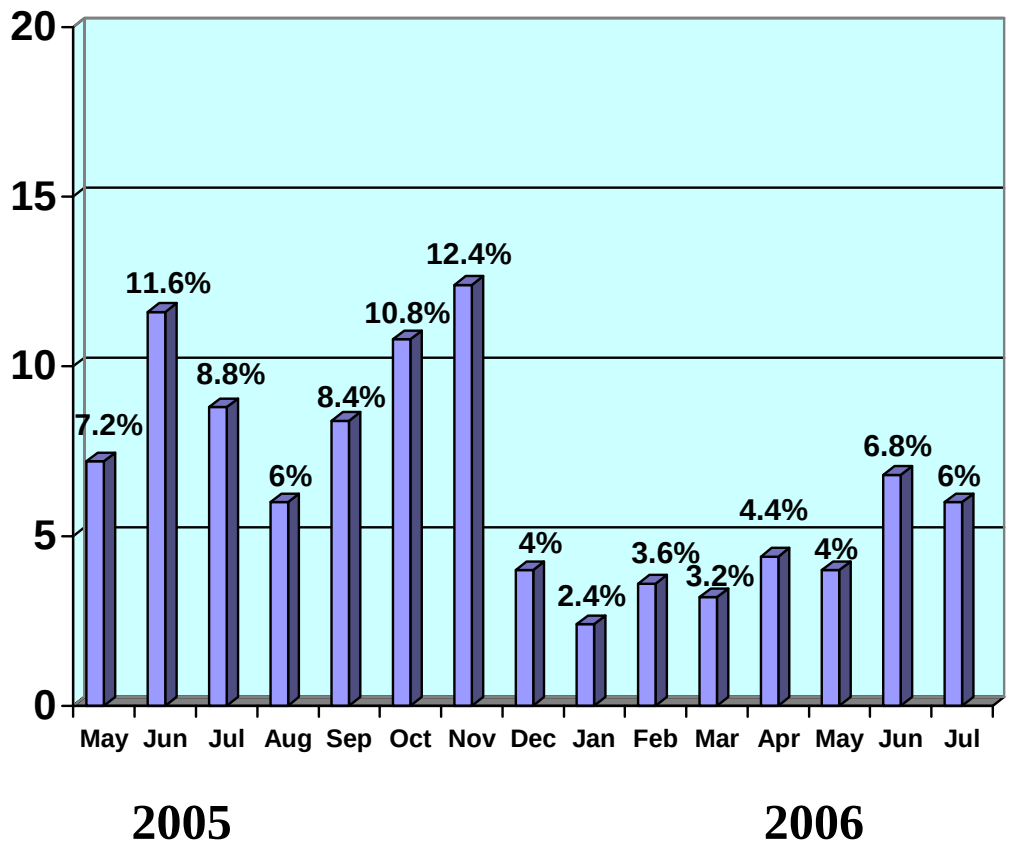
` **TABLE-2**

SEASONAL INCIDENCE IN OCCURANCE OF MALARIA

MONTH, YEAR	**PLASMODIUM VIVAX** (n-210)	**PLASMODIUM FALCIPARUM** (n-40)	**TOTAL** (n-250)%
May 2005	16	02	18 (7.2%)
Jun 2005	23	06	29 (11.6%)
Jul 2005	20	02	22 (8.8%)
Aug 2005	13	02	15 (6%)
Sep 2005	19	03	21 (8.4%)
Oct 2005	22	05	27 (10.8%)
Nov 2005	19	12	31 (12.4%)
Dec 2005	10	0	10 (4%)
Jan 2006	06	0	O6 (2.4%)
Feb 2006	09	0	09 (3.6%)
Mar 2006	06	02	08 (3.2%)
Apr 2006	08	03	11 (4.4%)
May 2006	10	0	10 (4%)
Jun 2006	15	02	17 (6.8%)
Jul 2006	14	01	15 (6%)

More than 50% of cases occurred during June and December 2005 which well correlate with monsoon in Chennai.

BAR CHART SHOWING SEASONAL VARIATION



Bar chart showing occurrence of malaria during monsoon and post monsoon in Chennai.

TABLE - 3

CLINICAL PROFILE OF PV AND PF MALARIA

CLINICAL FEATURES	PLASMODIUM VIVAX (n-210) %	PLASMODIUM FALCIPARUM (n-40)%	TOTAL (n-250)%
FEVER	210 (100%)	40 (100%)	250(100%)
CHILLS	183 (87%)	33 (82%)	216 (86.4%)
HEADACHE	152 (72%)	32 (80%)	184 (73.6%)
MYALGIA	45 (21%)	09 (23%)	54 (21.6%)
VOMITING	80 (38%)	23 (58%)	103(41.2%)
DIARRHEA	07 (3%)	01 (2%)	08 (3.2%)
ICTERUS	11 (5%)	17 (43%)	28 (11.2%)
SPLENOMEGALY	44 (21%)	15 (33%)	59 (23.6%)
HEPATOMEGALY	18 (9%)	06 (15%)	24 (9.6%)
LOC	25 (12%)	05 (13%)	30 (12%)
CONVULSION	14 (7%)	02 (5%)	16 (6.4%)

Fever occurred in all patients . Chills and headache were the commonest associated symptoms in more than 80% of the patients. Icterus and splenomegaly occurred more commonly in PF cases than in PV.

TABLE - 4

JAUNDICE : SERUM BILIRUBIN

TOTAL BILIRUBIN mg/dl	**PLASMODIUM VIVAX** (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
1.5 – 3 (Our Criteria)	12 (5.7%)	11(27.5%)	23 (9.2%)
> 3 (WHO Criteria)	12 (5.7%)	08 (20%)	20 (8%)
TOTAL	24 (11.4%)	19 (47.5%)	43 (17.2%)

MEAN BILIRUBIN - 5.3 mg/dl (RANGE 1.5 – 22)

TABLE - 5

TRANSAMINASES : SGOT

SGOT IU/L	**PLASMODIUM VIVAX** (n-24)	**PLASMODIUM FALCIPARUM** (n-19)	**TOTAL** (n-43)%
< 40	06	02	08 (18.6%)
40 - 80	12	09	21 (48.8%)
> 80	06	08	14 (32.6%)

MEAN SGOT - 82.67 IU/L (Range 17 – 238)

TABLE - 6

TRANSAMINASES: SGPT

SGPT IU/L	**PLASMODIUM VIVAX** (n-24)	**PLASMODIUM FALCIPARUM** (n-19)	**TOTAL** (n-43)%
< 40	04	02	06 (14%)
40 - 80	13	10	23 (53.5%)
> 80	07	07	14 (32.5%)

MEAN SGPT - 82.86 IU/L (Range 16 – 400)

Jaundice occurred in 17.2% of cases and its more common in Falciparum malaria (47.5%) than in Vivax malaria (11.4%). Maximum Bilirubin noted was 22 mg/dl. More than half of these patients had mild elevation in transaminases in the range of 40 to 80 IU/L.

A PATIENT WITH JAUNDICE AND RENAL FAILURE IN VIVAX MALARIA

TABLE - 7

RENAL FAILURE : SERUM CREATININE

SERUM CREATININE mg/dl	**PLASMODIUM VIVAX** (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
1.5 – 3 (Our Criteria)	12 (5.7%)	07 (17.5%)	19 (7.6%)
> 3 (WHO Criteria)	04 (1.9%)	03 (7.5%)	07 (2.8%)
TOTAL	16 (7.6%)	10 (25%)	26 (10.4%)

MEAN CREATININE - 2.6 mg / dl (Range 1.5 – 6.4)

TABLE - 8

RENAL FAILURE : SERUM UREA

UREA mg/dl	**PLASMODIUM VIVAX** (n-16)	**PLASMODIUM FALCIPARUM** (n-10)	**TOTAL** (n-26)
< 40	0	0	0
40 - 80	07	04	11 (42.3%)
> 80	09	06	15 (57.7%)

MEAN UREA - 99.5 mg / dl (Range 42 – 200)

Renal failure occurred in 10.4 % of cases as per our criteria but by WHO criteria its only 2.8%. Maximum Creatinine and urea noted was 6.4 mg/dl and 200 mg/dl.

TABLE - 9

CEREBRAL MALARIA

SYMPTOMS	**PLASMODIUM VIVAX** (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
LOC	13	04	17
GCTS & LOC	12	01	13
GCTS	02	01	03
TOTAL	27(12%)	06(15%)	33(13.2%)

TOTAL CEREBRAL MALARIA – 33

TOTAL LOC - 30 (90.9%)

TOTAL GCTS - 16 (48.5%)

Cerebral malaria occurred in 13.2% of cases. 90.9% of them had altered level of consciousness or altered behaviour where as generalized convulsions occurred in 48.5% of cases.

TABLE - 10

ANEMIA

HEMOGLOBIN g/dl	**PLASMODIUM VIVAX** (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
8 – 10	72 (34.3%)	10 (25%)	82 (32.8%)
5 – 8 (Our Criteria)	28 (13.3%)	09 (22.5%)	37 (14.8%)
< 5 (WHO Criteria)	01 (0.4 %)	02 (5%)	03 (1.2%)
TOTAL	101 (48.1%)	21 (52.5%)	122 (48.8%)

MEAN HEMOGLOBIN - 8.5g/dl

RANGE - 4.6 TO 10 g/dl

48.8% of cases had hemoglobin less than 10 g/dl. As per our criteria anemia occurred in 16% of cases where as by WHO criteria it is only 1.2%. the lowest hemoglobin noted was 4.6 g/dl.

COMBINATION OF COMPLICATIONS

TABLE - 11

ANEMIA WITH OTHER ORGAN DYSFUNCTION

ANEMIA Hb < 8g/dl **WITH**	**PLASMODIUM VIVAX** (n-29)	**PLASMODIUM FALCIPARUM** (n-11)	**TOTAL** (n-40)
RENAL FAILURE Sr Cr > 1.5 mg/dl	02	06	08 (20%)
JAUNDICE TB > 1.5 mg/dl	04	09	13 (32.5%)
CEREBRAL MALARIA	05	03	08 (20%)

Jaundice is the commonest complication associated with anemia which occurred in 32.5% of cases

TABLE - 12

JAUNDICE WITH OTHER ORGAN DYSFUNCTION

JAUNDICE WITH (TB > 1.5 mg/dl)	**PLASMODIUM VIVAX** (n-24)	**PLASMODIUM FALCIPARUM** (n-19)	**TOTAL** (n-43)%
ANEMIA Hb < 8g/dl	04	09	13 (30.2%)
RENAL FAILURE Sr Cr > 1.5 mg/dl	05	09	14 (32.5%)
CEREBRAL MALARIA	06	04	10 (23.3%)

Renal failure was the commonest complication associated with Jaundice.

TABLE - 13

CEREBRAL MALARIA WITH OTHER ORGAN DYSFUNCTION

CEREBRAL MALARIA WITH	**PLASMODIUM VIVAX** (n-27)	**PLASMODIUM FALCIPARUM** (n-06)	**TOTAL** (n-33)
ANEMIA Hb < 8g/dl	05	03	08 (24.2%)
RENAL FAILURE Sr Cr > 1.5 mg/dl	06	03	09 (27.3%)
JAUNDICE TB > 1.5 mg/dl	06	04	10 (30.3%)

Jaundice was commonly associated with cerebral malaria patients in 30.3%.

TABLE – 14

RENAL FAILURE WITH OTHER ORGAN DYSFUNCTION

RENAL FAILURE Sr Cr > 1.5 mg/dl WITH	**PLASMODIUM VIVAX** (n-16)	**PLASMODIUM FALCIPARUM** (n-10)	**TOTAL** (n-26)%
ANEMIA Hb < 8g/dl	02	06	08 (30.8%)
JAUNDICE TB > 1.5 mg/dl	O5	09	14 (53.8%)
CEREBRAL MALARIA	06	03	09 (34.6%)

Jaundice is the commonest complication associated with renal failure which occurred in 53.8% of cases.

TABLE - 15

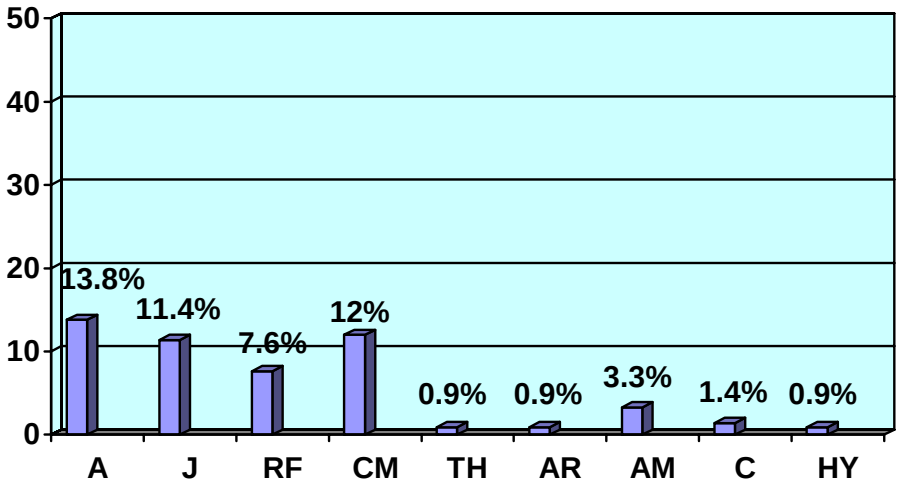
COMPLICATIONS

COMPLICATIONS	**TOTAL** (n-250)%	**PV** (n-210) %	**PF** (n-40)%	**Significance P value**
ANEMIA Hb < 8g/dl **WITH**	40 (16%)	29 (13.8%)	11 (27.5%)	0.03
JAUNDICE TB > 1.5 mg/dl	43 (17.2%)	24 (11.4%)	19 (47.5%)	0.001
RENAL FAILURE Sr Cr > 1.5 mg/dl	26 (10.4%)	16 (7.6%)	10 (25%)	0.001
CEREBRAL MALARIA	33 (13.2%)	27 (12%)	06 (15%)	0.7
THROMBOCYTOPENIA (PLATELET < 1 Lac)	04 (1.6%)	O2 (0.9%)	02 (5%)	0.06
ARDS SiO2 < 70%	03 (1.2%)	02 (0.9%)	01 (2.5%)	0.41
ALGID MALARIA/ HYPOTENSION	08 (3.2%)	07 (3.3%)	01 (2.5%)	0.78
CORTICAL VENOUS THROMBOSIS	03 (1.2 %)	03 (1.4%)	0	0.44
HYPOGLYCEMIA PL GLUC < 60	04 (1.6%)	02 (0.9%)	02 (5%)	0.06

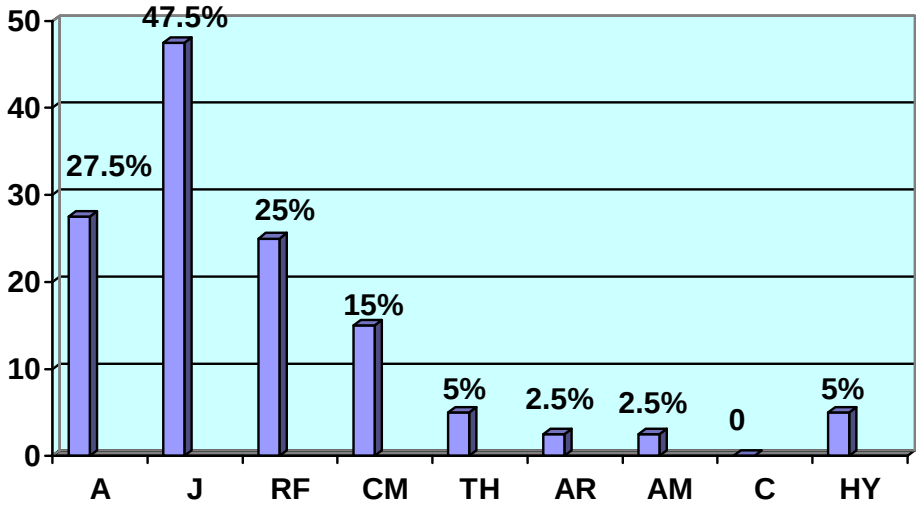
In falciparum malaria renal failure and jaundice is more common than cerebral malaria. The difference in incidence of jaundice and renal failure in PV & PF is statistically significant (p value 0.001) and there is no significant difference in incidence of other complications.

COMPARISON BAR CHARTS OF COMPLICATION IN PV & PF

COMPLICATION IN VIVAX MALARIA



COMPLICATION IN FALCIPARUM MALARIA



LEGENDS – A-Anemia, J - jaundice, RF – Renal failure, CM – Cerebral malaria, TH – Thrombocytopenia, AR – ARDS, AM – Algid malaria, C – CVT, HY – Hypoglycemia.

TABLE – 16

TREATMENT

DRUGS	**PLASMODIUM VIVAX** (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
CHLOROQUINE +DOXY	100 (47.6%)	06 (15%)	106 (42.4%)
QUININE +DOXY	62 (29.5%)	28 (70%)	90 (36%)
CHLORQUINE ↓ QUININE	44 (20.9%)	04 (10%)	48 (19.2%)
ARTEMISININ	04 (1.9%)	02 (5%)	06 (2.4%)

TOTAL NO. OF PATIENTS TREATED WITH CHLOROQUINE - 154

NO. RESPONDED TO CHLOROQUINE - 106 (68.8%)

NO. NOT RESPONDED (RESISTANT) - 48 (31.2%)

ARTEMISISNIN IS USED AS QUININE WAS CONTRAINDICATED IN 06 PATIENTS WHO HAD ISCHEMIC HEART DISEASE.

Quinine is found to be very effective in complicated and chloriquine resistant malaria. 31.2% of patients showed chloroquine resistance.

TABLE – 17

MORTALITY

PLASMODIUM VIVAX (n-210) %	**PLASMODIUM FALCIPARUM** (n-40)%	**TOTAL** (n-250)%
O3 (1.4%)	01(2.5%)	04 (1.6%)

Mortality of 1.6% is noted. 3 patients had vivax and one Falciparum. The cause of death were cerebral malaria in one case and MODS in other three patients.

DISCUSSION

DISCUSSION

In India, 2.5 to 3 million cases and 1000 deaths of malaria are reported annually.[2] Many consider this is an underestimate. Areas with more than 30% of PF cases are categorized as high risk. These include North East India, Orissa, Jharkand, West Bengal, Madhya Pradesh, Maharashtra & Andrapradesh. Tamil Nadu has reported 43,000 cases in 2003, out of which 70% of cases were from Chennai. Malaria is highly prevalent in places from North Chennai like Tondaiarpet, Washermanpet, Royapuram, Harbour, Mannady, Pattalam & Pulianthope. This study was undertaken at Stanley Medical college Hospital which is located in North Chennai. This study deals with clinical and laboratory profile of Malaria in North Chennai.

Total of 250 cases of Malaria admitted to Stanley Medical college hospital were analyzed. Plasmodium vivax occurred in 210 (84%) and plasmodium falciparum occurred in 40 (16%) patients. There were 170 (68%) males and 80 (32%) females. Mean age of presentation was 27.7 years (range 13 to 82 years). About 70% of patients were in the age group of 13 to 40 years. The parasitic profile noted was 84% PV & 16% PF where as the parasitic profile as per corporation of Chennai data is 94.6% PV & 5.4% PF . This difference is due to analysis of hospitalized patients in our study where only severely ill patients get admitted. Chennai corporation data is mainly from OPD cases. Hazra et al from Calcutta has reported 73.3% PV & 26.7% PF in their study of 225 cases.[11] Mehta et al from Orissa has reported 54.5% PV,

36.6% PF and 8.9% of mixed infection.[16] This shows that the parasitic profile is different in various places. Thus Tamilnadu is in low risk category.

CLINICAL FEATURES

100% patients had fever. Typical paroxysms occurred only in very few patients. Most of them had daily fever peaking once in a day. Fever was associated with chills in 86% of cases (87% of PV & 82% of PF). Head ache occurred in 73.6% of patients (72% of PV & 80% of PF). Head ache was severe and was consistently associated with onset of fever. Mohapatra et al from Orissa reported migrainous head ache of 4.5% in a study of 110 cases of vivax Malaria.[12]

Vomiting(41.2%), Diarrhea (3.2%), Clinical jaundice(11.2%), Myalgia(21.6%), Diarrhea (3.2%), Hepatomegaly (9.6%) and Splenomegaly (23.6%) were the other clinical manifestations noted. 21% of PV and 33% of PF patients had Splenomegaly. This is consistent with Hazra et al study, who had reported Splenomegaly in 18.18% of PV and 40% of PF cases.[11] Mohapatra et al had reported 6.3% of myalgia in their study of 110 cases of vivax malaria.[12]

In our study more than 50% of the cases occurred during June and December 2005 which well correlates with the monsoon season of Chennai. Maximum number of 31 cases were reported in the month of November 2005 when Chennai was in floods.

JAUNDICE

Jaundice is the commonest complication noted in our study. Serum bilirubin of more than 1.5mg occurred in 43 cases (17.2%). As per WHO criteria serum Bilirubin of more than 3mg/ occurred only in 8% of cases. Serum Bilirubin ranged from 1.5 to 22mg/dl. Bilirubinemia is predominantly direct. Jaundice occurred in 11.4% of PV and 47.5% of PF cases. This is consistent with a study from Calcutta ,in which hazra et al reported jaundice in 9.09% of PV and 40% of PF cases.[11] Harris VK et al from south India reported 37% of jaundice in Pf cases.[18] Kochar et al from Rajasthan has reported jaundice 58.85% of PF cases 2001. [8]

In respect of hepatic enzymes, SGOT was elevated in the range of 40-80 IU /L in 48.8% and more than 80IU/L in 32.6% of cases. Maximum SGOT level noted was 438 IU/L. 53.5% of jaundiced patients showed SGPT elevation in the range of 40-80 IU/L & 32.5% over 80IU/L. Nityanand et al from Haryana has reported mean SGOT & SGPT of 120 & 130 IU/L respectively in their study of 60 cases.[19] Kochar et al from Rajasthan has reported a range of SGOT & SGPT of 40-1120 IU/L and 40-1245IU/L respectively. [20]

In our study the maximum Bilirubin noted was 22mg/dl, SGOT 483 IU/L and SGPT 400. Bilirubinemia is predominantly direct and in most of the cases there is only mild elevation of transaminases. Out of 43 jaundiced patients 30% had Anemia, 32.5% had Renal failure and 23.3% had cerebral malaria.

RENAL FAILURE

Acute renal failure occurred in 10.4% of cases (Serum Creatinine >1.5mg/dl). As per WHO criteria (Serum Creatinine >3 mg/dl) ARF occurred only in 2.8% of cases. In our study ARF occurred in 7.6% of PV and 25% of PF cases. Severe renal failure (Serum Creatinine >3mg/dl) occurred in 1.9% of PV and 7.5% of PF cases. This is consistent with Kochar's reported incidence of 6.25% of ARF in PF cases in 2001.[8] Nityanand et al reported an incidence of 21% ARF in a study of 60 cases (PV 14 and PF 46). [19]

In our study it has been found that renal failure also occurs in PV malaria in significant numbers. This has been proved by Kochar in his study of 11 cases of complicated Vivax malaria by documenting presence of PV and absence of PF by genetic study (PCR).[9, 21, 22]

57.7% of ARF patients showed rise in urea >80 mg/dl and remaining in the range of 40 to 80 mg/dl. Maximum Creatinine noted was 6.4 mg/dl and urea 200 mg/dl. No patient was dialysed. One patient with ARF died who also had other complications like jaundice, Anemia and ARDS.

In India reported incidence of ARF in malaria is 17.8% from Delhi,17.2% from Orissa, 13% from Northeast India and 5.9% from Mumbai.[13] Before 1995 there were no reports of ARF due to malaria in Chennai, Since then it has become an important cause of ARF which contribute to 4.5% of ARF.[15] Prakash et al from Varanasi reported 93 cases (16.1%) (74 PF and 19 PV) of Malarial ARF out of 577 cases of ARF studied.[16] Other complications

noted among ARF patients were jaundice 53.8%, anemia 30.8% and cerebral malaria 34.6%.

CEREBRAL MALARIA

33 patients (13.2%) had neurological dysfunction in the form of altered sensorium, loss of consciousness and generalized convulsions. 17 patients (51.5%) had LOC, 13 (39.3%) had both LOC and convulsions, and 3 (9%) had only convulsions. Kochar reported generalized convulsions in 21.31% of 441 cases of cerebral malaria from Rajasthan.[10] 12.8% of PV and 15% of PF had cerebral malaria in our study. This is consistent with Kochar's reported incidence of 10.9% of cerebral malaria in PF cases in 2001.[8] Siginificant number of PV patients exhibited neurological dysfunction.[9]

Other complications noted in cerebral malaria patients were anemia 24.2%, renal failure 27.3% and raundice 30.3%. Kochar has reported 31.74% of jaundice, 9.09% of renal failure and 6.8% of severe anemia in his study of 441 patients of cerebral malaria.[10] One patient died due to cerebral malaria caused by plasmodium vivax.

ANEMIA

48.8% of patients had Hb <10g/dl. Considering Hb <8g/dl as severe anemia the incidence is 16% and by WHO criteria (Hb <5g/dl) the incidence is only 1.2%. The lowest Hb noted in our study was 4.6g/dl. 13.7% of PV and 27.5% of PF cases had Hb <8g/dl. This is consistent with Kochar's repoted incidence of severe anemia in 26.04% of PF cases.[8] Mean Hb noted was 8.5g/dl.

Other complications noted with severe anemia (Hb <8g/dl) were renal failure 20%, Jaundice 32.5% and Cerebral malaria 20%.

OTHER COMPLICATIONS

Thrombocytopenia (platelet <1Lac) occurred in 4 cases (1.6%), 2 (0.9%)in PV and 2 (5%) in PF. Kochar reported 5.7% of Thrombocytopenia in PF cases in 2001.[8]

ARDS developed in 3(1.2%) patients, 2(0.9%) in PV and 1(2.5%) in PF. All the 3 died. Kochar reported 3.01%of ARDS in PF cases in 2001.[8]

Algid malaria with profound hypotension occurred in 3.2% of cases, 3.2% in PV and 2.5% in PF. Kochar reported 5.26% of shock in PF cases in 2001.[8]

Hypoglycemia occurred in 4 cases (1.6%),2 in PV(0.9%) and 2 (5%) in PF. Kochar reported 2.07%of hypoglycemia in PF cases in 2001.[8]

Cortical Venous thrombosis occurred in 3 patients of Vivax malaria. One male and two female (Post Partal Period) had CVT. There are very few data regarding complications occurring in vivax malaria .

MODS

In recent past the incidence of cerebral malaria is found to be declining and the complicated malaria, most commonly presents as multiple organ dysfunction. The usual combination were severe anemia, jaundice, renal failure and ARDS. In our study, commonest combination noted was renal failure with jaundice which had occurred in 14 patients (5 PV and 9 PF). Dreaded

combination of anemia, renal failure, jaundice and cerebral malaria occurred in 2 patients (1 PV and 1 PF).

The WHO criteria for diagnosis of organ dysfunction in severe malaria is serum Creatinine and Bilirubin of more than 3 mg / dl. We had taken a criteria of > 1.5 mg/dl for early diagnosis of ARF and jaundice which would prompt aggressive management early and prevent mortality.

MORTALITY

Four patients died which accounts for 1.6% of mortality rate. 3 had PV and 1 had PF. One patient with PV died of cerebral malaria and all the other three deaths were due to MODS with ARDS. This is consistent with Kochar's findings of shift in cause of mortality from cerebral malaria to MODS (1994 to 2001).[8] Low mortality may be due to early detection of organ dysfunction and aggressive management.

TREATMENT

In our study uncomplicated malaria patients were given chloroquine and if the fever persists after full course of chloroquine, Quinine was given. 42.4% (100 PV and 6 PF) of cases responded to Chloroquine and Doxycycline. 36% (62 PV and 28 PF) of patients were started on quinine and Doxycycline as they had complications. In 48 patients, Chloroquine was switched over to quinine as they showed no clinical response. There were no treatment failures with

quinine. Artemisinin group of drugs were used in 6 patients in whom quinine was contra indicated.

47.6% of Vivax malaria responded to chloroquine. 29.5% of PV cases were treated with quinine and Doxycycline as they had complications. 70% of PF cases responded to quinine and Doxycycline. And only 6 PF cases (15%) responded to chloroquine.

Total of 154 patients treated with chloroqine , 106 (68.8%) responded and 48 patients (31.2%) were found to be resistant.

In our study quinine was found to be very effective in complicated malaria and PF patients. Early initiation of quinine resulted in reducing morbidity and mortality. In cerebral malaria quinine was very valuable leading to rapid recovery in one or two doses. Regarding side effects of quinine, vomiting was the commonest to be noted and other complications like QTc prolongation and ambylopia were not found in our study.

This study has highlighted that plasmodium falciparum contributes to 16% of malaria in Chennai. Complications occurred in vivax also. There was very good response to quinine and Doxycycline in complicated malaria. Mortality was low (1.6%). Early diagnosis of malaria, rapid evaluation for organ dysfunction and aggressive management was probably responsible for this low mortality.

SUMMARY

SUMMARY

- 250 patients of malaria were analyzed.210 (84%) had Plasmodium vivax and 40 (16%) had Plasmodium Falciparum.
- Complications of PF (n – 40) – Jaundice 47.5%, Anemia 27.5%, Renal failure 25%, Cerebral malaria 15%, ARDS 2.5%,Thrombocytopenia 5% and Hypoglycemia 5%.
- Complications of PV (n – 210) - Jaundice 11.4%, Anemia 13.8%, Renal failure 7.6%, Cerebral malaria 12.5%, ARDS, Thrombocytopenia and Hypoglycemia in two cases, CVT in three cases.
- Jaundice occurred in 11.4% of PV and 47.5% of PF cases. Mean Bilirubin noted was 5.3mg/dl, predominantly of direct bilirubinemia with mild elevations of transaminases in the range of 40 to 80 IU/L. This Shows that jaundice in malaria is predominantly of cholestatic in origin.
- Renal failure occurred in 7.6% of PV and 25% of PF cases. Overall renal failure occurred in 10.6% of malaria. Mean creatinine and urea noted were 2.6mg/dl and 99.5mg/dl respectively. 76% of ARF was mild (Serum Creatinine 1.5 to 3mg/dl)
- 48.8% of patients had Hb <10g/dl. Only three patients had Hb <5g/dl and 37 patients (14.8%) had Hb in the range of 5 to 8g/dl. 13.8% of PV and 23% of PF had Hb <8g/dl. Mean Hb noted was 8.5g/dl.
- Cerebral malaria occurred in 13.2% of cases. Predominant presentations were altered behaviour, loss of conciousness (51%) and Generalized convulsions (48%). 12.8% of PV and 15% of PF patients had cerebral malaria.
- Other complications are less common. They were ARDS 1.2%, Thrombocytopenia 1.6%, Hypoglycemia 1.6% and CVT 1.2%.

- 42.4% were treated with chloroquine and 36% were treated with quinine in combination with Doxycycline. 19.2% were found to be chloroquine non responsive and later switched over to quinine with good response.
- Artemisinin group of drugs used in six patients in whom quinine was contraindicated as they had ischemic heart disease.
- Mortality – Four patients (1.6%) died, Three (1.4%) in Vivax and One (2.5%) in Falciparum. MODS was the cause of death in three out of four patients and one died of cerebral malaria

CONCLUSIONS

CONCLUSIONS

- Plasmodium vivax occurred in 84% and Plasmodium falciparum in 16%.
- Jaundice 47.5% and Renal failure (25%) were the important complications in Plasmodium Falciparum where as cerebral malaria occurred only in 15%.
- All severe complications like jaundice(11.4%), renal failure(7.6%), cerebral malaria(12%), severe anemia(13.8%) and ARDS(1.2%) were noted in Plasmodium vivax though less common compared to Plasmodium falciparum.
- Early detection of organ dysfunction utilizing Serum Creatinine >1.5mg/dl, total bilirubin >1.5mg/dl and Hb <8g/dl is valuable in diagnosing complicated malaria early and starting aggressive management (Quinine and Doxycycline), thereby preventing further morbidity and mortality.

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PROFORMA

Name : **Age:** **Sex:**

IP No.

PV/PF

Clinical Features:

- Fever – Duration/paroxysm
- Chills
- Headache
- Vomiting
- Myalgia
- Hepatosplenomegaly
- Icterus
- Altered sensorium
- Convulsions
- Loss of consciousness
- Diarrhea

Laboratory profile

- Hemogram
- Renal function tests
- Liver function tests

- Plasma glucose.
- ECG
- Chest X Ray
- USG – Abd.

Treatment

- Chloquine
- Quinine
- Chloroquine changed to quinine
- Other drugs.